DETAILED ACTION

Response to Amendment

This Office Action is in response to the amendment submitted on 03/024/08. Claims 23, 29, 31-34, and 45-50 are currently pending in the application, with claims 24-28, 30, and 35-44 having being cancelled. Accordingly, claims 23, 29, 31-34, and 45-50 are being examined on the merits herein.

Receipt of the aforementioned amended claims is acknowledged and has been entered.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d) for foreign priority based on an application filed in France on 07/16/2002, which papers have been placed of record in the file.

Applicant's comments regarding the listing of an International Search Report in an IDS have been considered and are found persuasive. As a result, the new IDS containing the ISR submitted in the reply dated 03/24/08 has been initialed and returned to applicant.

Applicant's argument regarding the submission of the titles of each non-Patent literature has been fully considered but is not persuasive. According to the M.P.E.P. 707.05 (e), citation of a publication requires sufficient information in order to determine the identity and facilitate the location of the publication. Moreover, Examiner respectfully points out that a copy of each non-patent literature was provided to applicant with the applicable titles listed.

Applicant's argument with respect to the 35 U.S.C. § 112, second paragraph has been fully considered and is found persuasive. Given the aforementioned amendment of the claims, the rejection under 35 U.S.C. § 112, second paragraph is withdrawn.

Applicant's contention that Geffard in view of Pomerance does not render obvious applicant's claims is fully acknowledged but is not found persuasive. As Geffard teaches a method of treating neurodegenerative diseases including Charcot-Marie-Tooth disease using polylysine conjugates. Geffard further teaches that antioxidants such as vitamin C can be conjugated and used in the treatment. Pomerance, on the other hand, teaches that vitamin C can inhibit cAMP-dependent activation of p38-MAPK. While Geffard does not explicitly teach vitamin C as a cAmp as a regulator, Pomerance teaches vitamin C as a cAmp modulator, an inherent property of the compound. Thus, to one of ordinary of skill at the time of the invention would have found it obvious to utilize the polylysine conjugated vitamin C as a c-AMP regulator in the treatment of Charcot-Marie-Tooth disease given the disclosure of Pomerance. As a result,

Geffard in view of Pomerance render obvious applicant's claims as previously presented.

Applicant's argument with respect to Djoneidi et al. as failing to cure the deficiencies of Geffard has been considered but is not found persuasive. Djoneidi et al. was provided to demonstrate that type 1 Charcot-Marie-Tooth disease (CMT1) is characterized by PMP22-protein mutations and that its expression is regulated by cAMP. Thus, to one of ordinary skill at the time of the invention would have found it obvious to use vitamin C polylysine conjugate to regulate or reduce the expression of PMP-22 and treat CMT1as Djoneidi et al. teaches that C-Amp regulates the expression of PMP-22 protein in CMT1. Thus, Geffard in view of Pomerance and in further view of Djoneidi et al. render obvious claims 29 and 37-38.

Applicant's argument with respect to Austria et al. as failing to cure the deficiencies of Geffard has been considered but is not found persuasive. Austria et al. was provided to demonstrate that salts of vitamin C are more stable than vitamin C. Thus, to one of ordinary of skill in the art at the time of the invention to use the salt esters of vitamin C as Austria et al. teaches them as more stable than vitamin C. Consequently, Geffard in view of Pomerance in further view of Austria et al. render obvious claims 32-34.

For the foregoing reasons, the rejection of claims 23-38 under 103 (a) remains proper and is maintained. However, In view of applicant's amendment, the following modified 103 (a) Final rejections are being made.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23, 31, and 48 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Geffard (U.S. 6,114,388, previously submitted).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Geffard teaches a method of treating neurodegenerative diseases, infections, traumatic or toxic neuropathies, neurodegenerative diseases resulting

from genetic diseases or proliferative diseases with polylysine conjugates for enhanced drug targeting to tissues and therapeutic purposes (see abstract and column 11, preparation IV, claim 16 and col. 2, lines 9-19). Geffard further teaches that this method of treatment further provides the use of polylysine conjugated with the antioxidant vitamin C or its derivatives (i.e. synthetic or natural vitamin C derivative; instant claims 23 and 31; see column 3, lines 7-8 and column 5, lines 8-11). Furthermore, Geffard discloses that the conjugates of the invention may be particularly useful for diseases presenting neurodegenerative disorders including Charcot-Marie-Tooth disease (instant claim 23; see column 5, lines 45-49). Geffard also teaches that the composition can be administered in doses of 0.5 to 1 ml or from about 5 mg to about 60 mg of the of the active principle such as vitamin C (see col. 10-14 for hapten concentration). Geffard further teaches that ultimately the dosage depends on the nature and severity of the disease to be treated and on the patient's weight but (instant claim see col. 6, lines 1-6).

Geffard does not teach the exact unit dose of 1 to 6 grams of vitamin C or a derivative thereof.

Geffard, however, does teach that the dosage can vary depending on the severity of the disease and the patient's weight.

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the method of Geffard to treat Charcot-Marie-

Tooth disease since he teaches the treatment of neurological disorders including Charcot-Marie-Tooth disease with polylysine conjugates of vitamin C or its derivatives. Thus, given the teachings of Geffard, one of ordinary skill would have been motivated to utilize vitamin C or its derivatives polylysine conjugates to treat Charcot-Marie-Tooth disease with the reasonable expectation of providing a method with enhanced therapeutic effects in treating Charcot-Marie-Tooth disease.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Geffard (U.S. 6,114,388, previously submitted) as applied to claims 23, 31, and 48 in view of Djoneidi et al. (Gene, 2000, pg. 223-231, previously submitted).

The Geffard reference is as discussed above and incorporated by reference herein. However, Geffard does not address the treatment of type 1 Charcot-Marie-Tooth disease (CMT1).

Djoneidi et al. teaches that PMP22 is a major component of peripheral nerve myelin and represents about 5% of the total myelin sheath (see pg. 223, left col., Introduction, paragraph 1). Djoneidi et al. further teaches that the major form of Charcot-Marie-Tooth disease is CMT1a that is characterized by deletion, duplication or point mutations of the PMP22 protein (see Introduction, page 223-224 vs. instant claim 29) and which suggests aberrant myelin sheath formation.

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the method of Geffard to treat Charcot-Marie-Tooth type 1 patients as this form is the major form of Charcot-Marie-Tooth detected in patients. Given that Geffard teaches a method of treating peripheral neuropathy such as Charcot-Marie-Tooth disease with vitamin C polylysine conjugates, and Djoneidi et al. discloses that the major form of the aforementioned disease is CMT1a, one of ordinary skill would have been motivated to utilize the method of Geffard to treat CMT1a in light of the disclosure of Djoneidi et al. with the reasonable expectation of providing a successful therapeutic treatment that is able to regulate proper myelin sheath formation.

Claims 32-34, 46-47, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geffard (U.S. 6,114,388, previously submitted) as applied to claims 23, 31, and 48 in view of Austria et al. (J. of Pharm. Biom. Anal. 1997,Vol. 15, pgs. 795-801, previously submitted).

The Geffard reference is as discussed above and incorporated by reference herein. However, Geffard does not teach the treatment Charcot-Marie-Tooth disease with a vitamin C salts, esters, or metal salts of phosphorylated ascorbic acid.

Austria et al. teaches that ascorbic acid is well known in the art as extremely unstable which results in its degradation (see pg. 795, right col.

Austria et al. further teaches that vitamin C derivatives such as magnesium ascorbyl phosphate and ascorbyl palmitate (instant claims 32-34, 46-47, and 49) were found to be more stable than vitamin C in solution (see abstract and figures 3-4, pg. 79). Importantly, Austria et al. teaches that ascorbyl palmitate led to 27% after 2 months storage in the dark at room temperature (RT) while magnesium ascorbyl phosphate had over 75% recovery after 60 days storage (see pg. 799, left col. and fig. 3-4).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the method of Geffard with the ascorbic acid derivatives disclosed by Austria et al. since these derivatives are more stable and would be more suitable for pharmaceutical uses. Given that Geffard teaches a method of treating Charcot-Marie-Tooth disease with polylysine conjugate of vitamin C, and Austria et al. teaches that ascorbic acid derivatives are more stable in solution than ascorbic acid itself, one of ordinary skill would have been motivated to utilize the ascorbic acid derivatives of Austria et al. into the method of Geffard with the reasonable expectation of providing a method of treatment that is therapeutically effective due to the usage of stable pharmaceutical compositions.

Claims 45 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geffard (U.S. 6,114,388, previously submitted) as applied to claims 23, 31, and 48 in view of Austria et al. (J. of Pharm. Biom. Anal.

1997,Vol. 15, pgs. 795-801, previously submitted) as applied to claims 32-34, 46-47, and 49 in further view of Fujinami et al. (Chem. Pharm. Bull. 2001, Vol. 49, Issue 5, pgs. 642-644).

The Geffard and Austria references are as discussed above and incorporated by reference herein. However, Geffard and Austria do not teach the treatment Charcot-Marie-Tooth disease with a glucoside or galactosyl derivatives of vitamin C or with ascorbyl sulfates.

Fujinami et al. teaches that vitamin C (i.e. AA) is susceptible to thermal and oxidative degradation and therefore the use of derivatives with increased stability is preferred (see pg. 642, left col. paragraphs 1-2). Fujinami et al. further teaches that 2-O-α-D-glucopyranosyl-L-ascorbic acid (i.e. AA-2G) and ascorbic acid-2S as stable derivatives of vitamin C (see pg. 642, left col. paragraphs 1-2 and fig. 1). Importantly, Fujinami et al. teaches that AA-2G and AA-2S are promising medical AA derivatives that possessed radical scavenging activity comparable to ascorbic acid (i.e. vitamin C) suggesting that these derivatives are functional equivalents.

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the derivatives of Fujinami et al. into the method of Geffard since Fujinami et al. teaches that these derivatives are more stable and would therefore be more suitable for medical uses. Given the teachings of

Geffard and Austria et al., one of ordinary skill would have been motivated to utilize the ascorbic acid derivatives of Fujinami et al. into the method of Geffard with the reasonable expectation of providing a method of treatment that is therapeutically effective due to the usage of stable pharmaceutical compositions.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

06/16/2008

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617